REMARKS

This Reply is in response to the Office action issued on January 26, 2010. Claim 16 has been amended. Support for said amendment can be found throughout the specification.

I. Rejection under 35 U.S.C. 112, Second Paragraph

Claims 16-18,65,67, and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts that claim 16 recites the phrase, "of the same organ" for which no antecedent basis is found. The claims have been amended to provide antecedent basis and clarify the claims. Applicant respectfully requests that the Examiner withdraw the rejection.

II. Rejection under 35 U.S.C. 112, First Paragraph

A. The Examiner's Rejection

Claims 16-18,28-30, and 69 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a cancerous cell of the breast or a method of detecting breast cancer, the method does not reasonably provide enablement for a method of identifying or detecting any cancer. Applicant appreciates and thanks the Examiner for indicated that identifying a cancerous cell of the breast or the detection of breast cancer is enabled subject matter. Applicant has not presently amended the claims to limit the scope, but Applicant respectfully requests the Examiner consider the following arguments in support of enablement of a broad class of cancers.

The Examine asserts that the instant specification does not provide any guidance or working example when it comes to determining/detecting cancers of other origins. She further claims that cancer involves multi-factorial processes, involving cascades of biochemical processes. Consequently, a particular gene marker for a particular cancer does not always equate to its successful usage for determination of other types of cancers. In support of her position, the Examiner relies on Knuutila et al. (American Journal of Pathology, 1998, vol. 152, no. 5, pages 1107-1123), pointing to a table, Table 1, showing that an increase copy of the gene ABL, is found in a particular types of cancer - Chronic myeloid leukemia and that the gene, HSTF1, is found to be increased in breast cancer and esophageal carcinoma.

The Examiner then concludes that it is therefore it is complexly unpredictable as to whether a cancer gene marker found in single type of cancer could be used for determining the presence of other types of cancers. The Examiner asserts unpredictability from examples of expression of markers other than TRIP13 as relating to the unpredictability of using TRIP13 as a marker. The Examiner may not appreciate the role of TRIP13 in the present method and is asked to consider what Applicant and related art has taught as to the role of TRIP13 in cancer as discussed herein.

B. The Wands Factors

The Federal Circuit has articulated the legal test of enablement in the case of *In re Wands*, 858 F.2d 731, 8USPQ2d 1400, 1404 (Fed. Cir. 1988). In this case, the Federal Circuit described many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirement and

whether any necessary experimentation is "undue." These factors include but are not limited to: (A) the breadth of the claim; (B) the nature of the invention' (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quality of experimentation needed to make or use the invention based on the content of the disclosure. *Id.*

In deciding the case, the Federal Circuit concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." *Id.* at 1408. Also see MPEP § 2164.01(a). Accordingly, the Federal Circuit reasoned that it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the factors while ignoring one or more of the others. *Id.*

Applicant respectfully states that the determination of whether "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual consideration. *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404.

Weighing all the above noted factual consideration, Applicant maintains that once in possession of the instant specification, one of ordinary skill in the art would have been able to practice the instant claims without undue experimentation, because the TRIP13 expression is evident in cells other than breast cancer which make it a useful tool for the identification of chromosomal abnormalities. Therefore, one of ordinary skill in the art would have conveniently been able to practice the claimed invention.

1. BREADTH OF THE CLAIM

The instant claims are directed to method of detecting cancer by measuring TRIP13 expression. It is respectfully submitted that there is no requirement under 35 U.S.C, 37 C.F.R or the Manual of Patent Examining Procedure (hereinafter "MPEP") for a Patentee to describe all possible cell types for diagnosis of cancer where the specification and the prior art sufficiently enable one of skill in the art to make and use the invention. For at least such reasons reconsideration, Applicant has adequately met the requirement under 35 U.S.C 112, 1st paragraph.

2. THE NATURE OF THE INVENTION

The nature of the invention relates to diagnostic methods for cancer by detecting increased expression of the marker TRIP13. Specification provides ample background description about TRIP13 expression in cancer cells and, in some examples, the related co-expression of cell cycle and regulatory markers in the specification.

3. STATE OF THE PRIOR ART

The expression of various markers as a means of detecting cancer cells are known in the art. Gene markers for identifying cancer cells were well known at the time of filing of this application, but also the various markers disclosed in Example 3 as being co-expressed with TRIP13 were known to be involved in cancer. As the Examiner appreciates TRIP13 expresses is found to correlate to breast cancer. However, Applicant's respectfully request the Examiner consider TRIP13 as a tool to view the abnormalities associated more broadly with cancers.

As the Examiner is clearly aware and which appears to be a basis of the rejection, cancer is a genetic disease where genetically and morphologically masses of genetic material are

formed. The present invention seeks to use TRIP13 as a visualization tool for more broadly measuring cancer abnormalities at the chromosomal level, rather than morphological level or even the molecular level.

The state of the art related to using TRIP13, which is encoded by SEQ ID NO: 1 in the instant application, as a tool to measure cancers of various cell types is clear. By way of example, Applicant directs the Examiner to U.S. Publication No. 2007/0059697, filed by the same inventive entity. This publication relates to determining cancer related to other methods of diagnosing a cancerous or pre-cancerous condition. Within that publication is disclosed Table 1, derived from publically available data. Table 1 shows a listing of a plurality of Sequences and the chromosomal location where each can be found. The table also shows the cell type where probes to the related sequence can measure increased expression and increased chromosomal copy number. The publication at paragraph [0144] teaches that increased chromosomal copy number correlates to cancers of various types. Specifically, Table 1 discloses the following SEQ ID NO's which are co-located on the same chromosomal region as TRIP13: SEQ ID No:26 for breast cancer; SEQ ID NO: 356 for colon cancer; SEQ ID NO:579 for lung cancer; SEQ ID NO: 721 for prostate cancer; SEQ ID NO: 722 for prostate cancer; SEQ ID NO: 833 for lung cancer; SEQ ID NO:834 for lung cancer; SEQ ID NO: 855 for prostate cancer; SEQ ID NO: 856 for prostate cancer. See US Publication 2007/0059697, paragraph [0144] and Table 1. Since these sequences and probes drawn thereto are on the same chromosomal region as TRIP13, increased copy number as claimed could be measured in various cell types such that various cancer types can be identified.

Applicant asks the Examiner to step back from the reading of the claims as set forth in the Office action of January 26, 2010 and to consider TRIP13 as the tool to visualize chromosomal abnormalities that are indicative of cancer broadly. For the foregoing reasons, probes to TRIP13 which measure increased chromosomal copy number through known methods such as FISH or flow cytometry would therefore cancers of a broad type as claimed by Applicant.

Pursuant to such evidence, Applicant respectfully submits that one of ordinary skill in the art would have been able to practice the scope of the claimed invention, once in possession of the instant specification. For such reasons alone, Applicant requests withdrawal of this rejection.

4. THE LEVEL OF ONE OF ORDINARY SKILL

The relative skill in the art relates to routine practices of the skilled worker in the field of molecular biology. Accordingly, those of ordinary skill in the art are highly trained in the field of molecular diagnostics and clinical applicability.

5. THE LEVEL OF PREDICTABILITY IN THE ART

It has been well settled that the amount of guidance or direction needed to enable the invention is inversely related to the amount of the knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Accordingly, the more that is known in the art, the more predictable the art is, and the less information needs to be explicitly stated in the specification.

As described above, there are ample information in the art about TRIP13, gene markers co-expressed with TRIP13 and cancer diagnostics. Also, the level of those of skill in the art is advanced. Thus, consistent with the state of law, there is no need for the applicant to articulate

material already known in the art. Applicant submits that the teachings of specification is sufficient for those of ordinary skill in the art who would have been interested is identifying various cancer cell types using TRIP13 as a marker.

6. THE AMOUNT OF DIRECTION PROVIDED BY THE INVENTOR;

Inventors have provided more than 45 pages describing how to diagnose cancer including breast, colon and lung. The inventors have described TRIP13 in detail and the method of using probes to TRIP13 to measure chromosomal aneuploidy.

Applicants direct the Examiner to page 13, line 5 and page 14, lines 15-30 which discloses that TRIP13 expression can be used as a diagnostic marker for breast, colon, lung and prostrate malignancies. Further in Example 3, Applicants show use of the Affymetrix U133 chipset which includes breast cancer and other cancer samples.

Separately, Example 3 discloses that several genes were found to be co-expressed with high levels of TRIP13 expression, those include genes involved in mitotic spindle assembly, kinetocore function, and chromosome function and maintenance. Various references show where these genes are highly expressed, they can be considered markers for cancers other than breast cancer. Tomonaga et al. (*Cancer Research* 63, 3511-3516, July 1, 2003) teach that chromosome missegregation during mitosis is the main cause of aneuploidy and contributes to oncogenesis and that CENP-A was overexpressed in all of 11 primary human colorectal cancer tissues. Whitfield et al. (Mol Biol Cell. 2002 June; 13(6): 1977–2000) show increased expression of KNSL5 in HELA cells.

Accordingly, based on this disclosure and the knowledge already available in the prior art, one skilled in the art in possession of such teachings would understand how to make and use

the invention for the identification of cancer cells. The amount of direction provided by the inventors has met the requirement under 112, 1st paragraph.

7. THE EXISTENCE OF WORKING EXAMPLES

The instant specification of replete of working example including Example 3, described in detail herein. The present specification provides 4 working examples to convey to those of ordinary skill in the art how to make and use the invention.

8. THE QUALITY OF EXPERIMENTATION NEEDED TO MAKE OR USE THE INVENTION BASED ON THE CONTENT OF THE DISCLOSURE.

With respect to the quality of experimentation needed, the Federal Circuit has stated that "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the directions in which the experimentation would proceed." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The present specification provides ample description of how to make and use the invention. As the Federal Circuit has described, considerable quantitative experimentation is not considered undue. Therefore, for at least such reasons the rejection should be withdrawn because the quality of such experimentation would have been routine where the skills of those of skill in the art is high and where such unpredictability in the art is low given the disclosure of the specification and the knowledge set forth in the prior art.

C. Applicants' Conclusion In View Of The Foregoing

In particular, the Examiner has failed to show, the unpredictability of the art for correlating increased chromosomal aneuploidy, measured by TRIP13, to cancer. Indeed, the

Examiner agrees as to breast cancer cells this correlation is predictable. Since cancer is a genetic disease and other markers known to on the same chromosome region as TRIP13 are associated with various cancers, TRIP13 as a probe target to measure aneuploidy in cells would be predictable in view of the art and the disclosure herein. Therefore, Applicant has taught those of ordinary skill in the art to make and use the present invention. Applicant respectfully submits that the full scope of the claims are enabled where the copy number of TRIP13 is used as a cancer diagnostic marker, where as claimed a normal same of the same tissue source material when compared with TRIP13 shows increased chromosomal copy. It is clear that one of skill in the art could easily make and use the present invention.

Therefore, the art is not highly unpredictable and based on the knowledge set forth in the prior art and the disclosure herein, Applicant's invention is enabled for the full scope of the claims as filed. Therefore, Applicant's respectfully request the Examiner withdraw the present rejection.

Applicant respectfully submits that the current disclosure adequately describes the method of practicing the invention. Considering the scope of claims and the description of the current disclosure, together with the predictability of the state of art, and the general level of one of ordinary skill in the art, Applicant maintains that the specification meets the enablement requirements set forth under 35 U.S.C, 112, 1st paragraph.

III. Conclusion

In view of the foregoing, Applicant submits that the claims pending in the application, are in condition for allowance. The Examiner is respectfully requested to pass the above application to issue at the earliest possible time. Should the Examiner find the application to be other than in

condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary.

Applicant hereby petitions for an Extension of Time to reply within the third (3rd) month and hereby submits payment in the amount of $555.00 for such extension. Applicant requests any extension of time necessary for entry of this Response. The commissioner is authorized to charge any required fees ("small entity" status) to Deposit Account No. 50-4364, from which the undersigned is authorized to draw.

Respectfully Submitted,

/Konstantina M. Katcheves/

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